

CLAIMS

What is claimed is:

1. A method of monitoring the accumulation of a compound of interest at a desired site *in vivo* by magnetic resonance imaging, the method comprising:
 - (a) administering to a subject a non-sensitive liposome composition comprising:
 - (i) a contrast agent;
 - (ii) a compound of interest; and
 - (iii) a non-sensitive liposome encapsulating the contrast agent and the compound of interest; and
 - (b) monitoring the accumulation of the compound of interest at the desired site by magnetic resonance imaging.
2. The method of claim 1, comprising increasing blood flow to a desired site.
3. The method of claim 2, wherein the increasing blood flow is by a method selected from the group consisting of contacting a heated material with the desired site, applying RF energy to the site, applying ultrasonic energy to the site and applying a laser beam to the site.
4. The method of claim 1, wherein the desired site is selected from the group consisting of a tumor, injury site, and tissue edema.
5. The method of claim 1, wherein the non-sensitive liposome comprises DSPC/Cholesterol (55:45, mol:mol).
6. The method of claim 1, wherein the contrast agent comprises a element selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni, Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn.

7. The method of claim 1, wherein the compound of interest is a chemotherapeutic agent.

8. An *in vivo* method of monitoring the localization and distribution of a compound of interest to a desired site in an organism by magnetic resonance imaging, the method comprising:

- (a) administering an envirosensitive liposome composition to a subject, the composition comprising:
 - (i) a contrast agent;
 - (ii) a compound of interest; and
 - (iii) an envirosensitive liposome encapsulating the contrast agent and the compound of interest; and
- (b) monitoring the localization and distribution of the compound of interest to a desired site by magnetic resonance imaging.

9. The method of claim 8, further comprising increasing blood flow to the desired site.

10. The method of claim 9, wherein the increasing blood flow comprises heating the desired site.

11. The method of claim 10, wherein the increasing blood flow is by a method selected from the group consisting of contacting a heated catheter with the desired site, applying RF energy to the site, applying ultrasonic energy to the site, applying a laser beam to the site.

12. The method of claim 8, wherein the envirosensitive liposome is a liposome selected from the group consisting of a thermosensitive liposome, a pH-sensitive liposome, a chemosensitive liposome and a radiation-sensitive liposome.

13. The method of claim 8, wherein the desired site is a tumor.

14. The method of claim 12, wherein the thermosensitive liposome comprises a formulation selected from the group consisting of DPPC-PEG₂₀₀₀, DPPC-DSPE-PEG₂₀₀₀ (95:5, mol:mol); DPPC-MSPC-DSPE-PEG₂₀₀₀ (90:10:4, mol:mol).

5

15. The method of claim 8, wherein the contrast agent comprises a element selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni, Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn..

10 16. The method of claim 8, wherein the compound of interest is a chemotherapeutic agent.

15 17. The method of claim 8, further comprising exposing the envirosensitive liposome at the desired site to a non-physiological environmental condition.

18. The method of claim 17, wherein the environmental condition is selected from the group consisting of hyperthermia, electromagnetic radiation, a chemical agent and non-physiological pH.

20

19. A method of detecting an *in vivo* blood pool, the method comprising:

- 25 (a) administering a liposome composition to a subject, the composition comprising:
- (i) a contrast agent; and
- (ii) a liposome encapsulating the contrast agent;
- (b) generating a magnetic resonance image of a site of interest; and
- (c) detecting the presence of an *in vivo* blood pool by analyzing the magnetic resonance image.
- 30

20. The method of claim 19, wherein the liposome composition comprises a non-sensitive liposome composition.

21. The method of claim 20, wherein the non-sensitive liposome comprises DSPC/Cholesterol (55:45, mol:mol).

5 22. The method of claim 19, wherein the liposome composition comprises an envirosensitive liposome composition.

23. The method of claim 22, wherein the envirosensitive liposome composition is selected from the group consisting of a thermosensitive
10 liposome composition, a pH-sensitive liposome composition, a chemosensitive liposome and a radiation-sensitive liposome composition.

24. The method of claim 23, wherein the thermosensitive liposome composition comprises a formulation selected from the group consisting of
15 DPPC-PEG₂₀₀₀, DPPC-DSPE-PEG₂₀₀₀ (95:5, mol:mol); DPPC-MSPC-DSPE-PEG₂₀₀₀ (90:10:4, mol:mol).

25. The method of claim 19, wherein the contrast agent comprises a element selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni,
20 Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn.

26. The method of claim 19, wherein the site of interest comprises a structure selected from the group consisting of a tumor, an embolism, an ischemia, an injury site, and a tissue edema.

25

27. The method of claim 19, wherein the analyzing comprises examining the image to detect the presence of an accumulation of contrast agent, wherein an accumulation of contrast agent indicates the presence of a blood pool.

30

28. The method of claim 27, wherein the examining comprises making a pixel density determination.

29. A method of monitoring the accumulation of a compound of interest at a desired site *in vivo* by magnetic resonance imaging, the method comprising:

- 5 (a) administering to a subject an envirosensitive liposome composition comprising:
- (i) a contrast agent;
 - (ii) a compound of interest; and
 - (iii) an envirosensitive liposome encapsulating the contrast agent and the compound of interest; and
- 10 (b) monitoring the accumulation of the compound of interest at a desired site by magnetic resonance imaging.

30. The method of claim 29, wherein the site of interest is selected from the group consisting of a tumor, injury site, and tissue edema.

15

31. The method of claim 29, wherein the envirosensitive liposome is a liposome selected from the group consisting of a thermosensitive liposome, a pH-sensitive liposome, a chemosensitive liposome and a radiation-sensitive liposome.

20

32. The method of claim 31, wherein the thermosensitive liposome comprises a formulation selected from the group consisting of DPPC-PEG₂₀₀₀, DPPC-DSPE-PEG₂₀₀₀ (95:5, mol:mol); DPPC-MSPC-DSPE-PEG₂₀₀₀ (90:10:4, mol:mol)

25

33. The method of claim 29, wherein the contrast agent comprises an element selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni, Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn.

34. The method of claim 29, wherein the compound of interest is a chemotherapeutic agent.

30

35. A method of generating a heating profile of a site of interest, the method comprising:

- (a) administering to a subject a thermosensitive liposome composition comprising:
 - 5 (i) a contrast agent; and
 - (ii) a thermosensitive liposome encapsulating the contrast agent and the compound of interest and having a melting temperature T_m ;
- (b) heating a site of interest in a subject;
- 10 (c) monitoring release of the contrast agent from the thermosensitive liposome using magnetic resonance imaging; and
- (d) generating a heating profile of the site of interest, wherein heating of an area to a temperature of at least T_m is indicated by release of contrast agent.
- 15

36. The method of claim 35, wherein the thermosensitive liposome comprises a formulation selected from the group consisting of DPPC-PEG₂₀₀₀, DPPC-DSPE-PEG₂₀₀₀ (95:5, mol:mol); DPPC-MSPC-DSPE-PEG₂₀₀₀ (90:10:4, mol:mol)

20

37. The method of claim 35, wherein the contrast agent is selected from the group consisting of Gd, Cu, Cr, Fe, Co, Er, Ni, Eu, Dy, Zn, Mg, Mo, Li, Ta, and Mn.

25

38. The method of claim 35, wherein the heating is by a method selected from the group consisting of contacting a heated material with the site of interest, applying RF energy to the site, applying ultrasonic energy to the site and applying a laser beam to the site.

30

39. The method of claim 35, wherein steps (a)-(c) are repeated a desired number of times.

40. The method of claim 39, wherein two or more thermosensitive liposomes are employed, each having a different T_m .